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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/568,332	02/13/2006	Gunter Stempfer	BP/G-33315A/BCK	6279

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EXAMINER	
WEGERT, SANDRA L	
ART UNIT	PAPER NUMBER
1647	
MAIL DATE	DELIVERY MODE
08/18/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/568,332	STEMPFER ET AL.	
	Examiner	Art Unit	
	SANDRA WEGERT	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *01 May 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-23* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-12 and 20* is/are rejected.

7)☒ Claim(s) *13-23* is/are objected to.

8)☒ Claim(s) *1-23* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *7/5/06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Detailed Action

Status of Application, Amendments, and/or Claims

The Information Disclosure Statement, sent 5 July 2006, has been entered and considered. Applicants' election of the species of (a) E. coli, and (b) an Interferon, in the Paper of 1 May 2008, is acknowledged. Applicants traversed the Restriction, arguing essentially that the unifying technical feature of the bacteria species is the presence of a periplasm into which peptides are secreted, while the unifying technical feature of the proteins cited are that they can be produced by the claimed method. However, the species of bacteria claimed and species of peptides claimed have not been shown to possess a single unifying feature by the applicants, or by anyone else. While it is true that the gram-negative bacteria cited generally are thought of as having large periplasms, there is no evidence that all the bacteria cited in the claims, aside from E. coli, would function in a suitable way in the claimed method. And in fact, applicants make no mention of bacteria besides E. coli in the Disclosure. Likewise, the types of polypeptides transported by the periplasmic pumps have not been characterized even within a species, much less in bacteria as a group (see Pages, et al, 2005 for a review). Applicants are reminded that, upon allowance, the first enabled method of using the claimed compounds will be rejoined to the examined Invention, if it too is free of the art. Accordingly, the restriction requirement is deemed proper and is made final.

Claims 1-23 are under examination in the Instant Application.

Claim Rejections/Objections

Claim Objections-

Claim 13 and dependent claims 14-23 are objected to as failing to provide proper antecedent basis for the claimed subject matter. See 37 CFR 1.75(d)(1) and MPEP § 608.01(o). Correction of the following is required: In claim 13, the following generic method steps *in sequence,* cannot be found in the specification as filed:

(i) cation exchange chromatography,

(ii) anion exchange chromatography,

(iii) hydrophobic interaction Chromatography,

(iv) cation exchange chromatography, and

(v) size exclusion chromatography.

Claim Rejections- 35 USC § 112, second paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> **The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.**

Claim 20 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 20 recites the limitation "said prokaryotic host," referring to claim 13, from which it depends. There is insufficient antecedent basis for this limitation in the claim, since claim 13 does not refer to use of a host or bacterium.

Claim Rejections- 35 USC § 102

The following is a quotation of the appropriate paragraph of 35 U.S.C. 102 that forms the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless -

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 1-10 are rejected under 35 U.S.C. 102(b) as being anticipated by Bochner et al (1987, US Patent 4,680,262). Bochner et al disclose a method for the preparation of human Growth Hormone (hGH) from transformed E. coli cells, said method comprising culturing a transformed E. coli culture in 500 mL LB medium and tetracycline at 37 °C for 8hrs. The reference describes the process as "fermentation", meaning the cells are cultured at 37 °C and pH 7.5 for 36 hours, after which steam is immediately injected into the fermenter jacket, the temperature of the tank rises rapidly to 50 °C, and the high temperature is held for 10 minutes

(Example 8, column 12). During this time hGH is secreted into the *periplasm* of the transformed E. coli host cells (see Title and Abstract) as required by the instant independent claims. In addition, the reference discusses extraction of the polypeptide of interest by osmotic shock (column 2, line 46), as recited in claims 1 and 2 and encompassed by all claims. In addition, Bochner et al discuss agents used for osmotic shock, such as sucrose (column 5, line 32), as well as typical concentrations used, such as 20% sucrose, as recited in claims 3-6. Terms specific to Claims 7-10 are disclosed throughout the reference: the bacteria are Gram-negative (Column 1, line 48); the host cell used was E. coli (see Example 1); and the reference discloses a method of producing growth hormone or any peptide of interest (column 1, paragraph 4), as recited in claim 10. Accordingly, the teachings of Bochner et al meet every limitation of the instant broad claims.

Claims 1-12 are rejected under 35 U.S.C. 102(e) as being anticipated by Kwon et al (US 2004/0151695 A1). Kwon et al disclose a method for producing human interferon alpha, including human interferon alpha 2A (as required by claims 10-12), by recombinantly expressing and secreting the same into the periplasm (as required by claims 1-12) of a genetically modified *E. coil* (see at least the abstract; paragraph 33, Fig. 5a and 5b and Examples 1-3). In an exemplification, Kwon et al teach that following the induction of IPTG for 3 hours, *E. Coli* transformants were centrifuged at 6,000 rpm for 20 minutes to precipitate the bacterial cells, and the precipitate was suspended in a 1/10 volume of isotonic solution (20% sucrose (see claims 3-6), 10 mM Tris-HCI buffer containing l mM EDTA, pH7.0), and the suspension was allowed to stand at room temperature (about 20-25 °C) for 30 minutes, and then centrifuged to collect

bacterial cells (example 3). All of these steps are prior to the step of resuspension of the collected bacterial cells in distilled water at 4 °C to extract proteins by osmotic shock (as required by claims 1-12) present in the periplasm of the cells; they therefore constitute the interrupting steps prior to extraction (see example 3, particularly paragraphs 69-70). Therefore, the teachings of Kwon et al meet every limitation of claims 1-12.

Conclusion: Claims 1-12 and 20 are rejected for the reasons recited above. Claims 21-22 are objected to as depending upon a rejected claim. Claims 13-23 are objected to for lack of antecedent basis in the specification.

Advisory information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sandra Wegert whose telephone number is (571) 272-0895. The examiner can normally be reached Monday - Friday from 9:00 AM to 5:00 PM (Eastern Time). If attempts to reach the examiner by telephone are unsuccessful, the Examiner's supervisor, Manjunath Rao, can be reached at (571) 272-0939.

The fax number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you

would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (in USA or CANADA) or 571-272-1000.

/SLW/
13 August 2008

/Marianne P. Allen/
Primary Examiner, Art Unit 1647